IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant: Luciano, Joanne Sylvia
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Examiner: Solis
Title: A Method for Predicting the Therapeutic Outcome of a Treatment for an Affective Disorder

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Assistant Commissioner of Patents
Box Patent Applications
Washington, DC 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with the provisions of 37 CFR Sections 1.56, 1.97, and 1.98, Applicant hereby submits copies of the documents shown on the attached PTO-1449 form, for consideration by the Examiner, in connection with the examination of the above-identified patent application.

It is respectfully requested that each of the Documents AA-AF and AR-CI be considered and made of record in this application.

AA. US Patent No. 5,708,591 (Givens) discloses a method and an apparatus for predicting the presence of congential and acquired imbalances and therapeutic conditions associated with thrombosis/hemostasis from at least one time dependent measurement to provide a time dependent profile. In one embodiment a neural network model which is trained is used to predict the existence of a therapeutic condition in an unknown sample.

AB. US Patent No. 5,701,394 (Arita et al.) discloses an information processing system having a neural processing unit, an expert system for executing an inference using a rule, and an information selection unit for improving the certainity of the information to be selected.

AC. US Patent No. 5,598,509 (Takahashi et al.) discloses a method of configuring a neaural network and a diagnosis / recognition system using the same.

AD. US Patent No. 5,591,588 (Goldstein et al.) discloses a method for the diagnosis or confirmation of the diagnosis of depression based upon monitoring blood levels of arginine vasopressin and / or thymopoietin for increases in the blood levels thereof.

AE. US Patent No. 5,295,197 (Takenaga et al.) discloses an information processing system using a neural network learning function.

AF. US Patent No. 5,222,194 (Nishimura) discloses a neural network computation apparatus having a plurality of layers, each having at least an input layer and an output layer. Each layer has a plurality of units and of links. The links connect the units on the layers. Also present is a means for changing the input and output charateristics of a particular unit and / or the weight of a particular link in accordance with an output after

learning an example and with a particular rule.

AR. Aboul-Saleh, M. T. And Coppen, A. (1983). Classification of depression and response to antidepressive therapies. *British Journal of Psychiatry*, 143: 601-603 discusses the results of treating patients diagnosed with depression with electroconvulsive shock, with medication, and with lithium..

AS. Bowden, C., et.al.; (1993). Fluxetine and despiramine in major depressive disorder. *Journal of Clinical Psychopharmacology* 13: 305-311 discusses the results of treating patients diagnosed with depression with fluoxetine and desipramine.

AT. Bryson, A.E. and Ho, Y.-C.; (1975) *Applied Optimal Control* , Hemisphere Publishing Co., New York, pp. 42-89 discusses optimization problems for dynamic systems.

AU. Bryson, A.E. And Ho, Y.-C. (1969) *Applied Optimal Control.* Blaisdell, New York (will be provided under separate cover) provides background on a mathematical method.

AV. Carney, M., et. Al. (1986) Prediction of outcome in depressive illness by the newcastle diagnosis scale: Its relationship to with the unipolar/bipolar and DMS-III systems. *British Journal of Psychiatry 150: 43-48* discusses the distribution of Newcastle scores from severely depressed inpatients.

AW. deBoor, □C.; (1978)*A practical guide to splines* , Springer-Verlag (will be provided under separate cover) provides background on a mathematical method.

AX. Efron, B. (1982) *The Jackknife, the bootstrap, and other resampling plans.* Society for Industrial and Applied Mathematics, Philadelphia, PA, Table of Contents. This reference provides background information on a mathematical method.

AY. Efron, B. And Tibshirani, R. (1991) Statistical data analysis in the computer age. *SCIENCE* 253: 390-395 discusses new statistical methods for use with computers.

AZ. Elkin, I., et.al. (1989) National Institue of Mental Health treatment of depression collaborative, *Archives of General Psychiatry* 46: 971-983 discusses the effectiveness of two types of psychotherapy.

BA. Filip, V., et. al. (1993) Predicting therapeutic results with levoprotiline and maprotiline in major depression: The role of the outcome criteria. *British Journal of Psychiatry*, 163: 35-38 discusses the results of a study wherein patients having depression were treated with levoprotiline or maprotiline and the results of several prediction analyses (delta score v. Ratio score v. Final score).

BB. Grossberg, S.; (1982) *Studies of Mind and Brain* , D. Reidel, Dordecht, Holland, pp. 74-79 discusses aspects of neural net mathematical systems.

BC. Hamilton, M. (1960) A rating scale for depression. *Journal of Neurological and Neurosurgical Psychiatry* 23: 56-62 provides a rating scale for measuring symptoms of depression.

BD. Hamilton, M. (1967) Development of a rating scale for primary depression illness. *British Journal of Social and Clinical Psychiatry* 8: 278-298 (will be provided under separate cover) provides a rating scale for depression which is based upon observable symptoms.

BE. Hinrichsen, G., et. al. (1993) Factors associated with recovery from and relapse into major depressive disorder in the elderly. *American Journal of Psychiatry*, 150: 1820-1825 researched factors in elderly depressed patients in order to ascertain which one were related to the patient's recovery.

BF. Hoencamp, E., et. al.;(1994) Predictors of (non-) response in depressed outpatient treated with a three-phase sequential mediation strategy. *Journal of Affective*

*Disorders*, 31:235-246 evaluated the predictive value of eight sets of variables in depressed outpatients.

BG. Hull, J.W., et.al.; (1993) Time series analysis of inervention effects, fluoxetine therapy as a case illustration. *Journal of Nervous and Mental Disease* 181: 48-53 illustrates the advantages of a time series analysis in documenting treatment effects using a case study of one patient.

BH. Johnson, S.L., et. al. (1994) Clinical characteristics associated with interpersonal depression: symptoms, course, and treatment response. *Journal of Affective Disorders*, **31**: 97-109 researches the relationship between interpersonal depression and major depression.

BI. Joyce, P.R., et.al. (1994). Temperament predicts clomipramine and despramine response in major depression. *Journal of Affective Disorders* 30: 35-46 investigated the predictive value of temperament on the response to treatment with antidepressant drugs in depressed patients.

BJ. Joyce, P.R. And Paykel, E. (1989) Predictors of drug response in depression. *Archives of General Psychiatry* 46: 89-99 provides a review of certain predictors of response to antidepressant drugs.

BK. Katon, W., et. al. (1994) The predictors of depression in primary care. *Journal of Affective Disorders*, 31: 81-90 provides a multivariate analysis to determine the predictors of persistenceof affective symptoms.

BL. Katz, M., et.al.; (1987) The timing, specificity, and clinical predictors of tricyclic drug effects in depression. *Psychological Medicine* 17: 297-309 describes research aimed at studying the rate of tricyclic drugs in depressive disorders.

BM. Kocsis, J.H., et. Al. (1989) Prediction of response of chronic depression to imipramine. *Journal of Affective Disorders* 17: 225-260 discusses results of imipramine treatment for chronic depression.

BN. Lehmann, E.L. (1986). *Testing statistical hypotheses*. Wiley Series in Probability and Mathematical Statistics, Wiley, New York (will be provided under separate cover) provides background information on the mathematics of testing statistical hypotheses.

BO. Luce, R.D., et. al. (1990) *Foundations of Measurement*, volume 1: Additive and polynomial representations. Academic Press, Inc., New York, pp. 454-544 provides background information on mathematical methods.

BP. Luce, R.D. (1990). *Foundations of Measurement*, vol. 3: Representation, axiomatization, and invariance. Academic Press, Inc., New York, pp. 267-337 provides background information on mathematical methods.

BQ. McGrath, P.J., et.al. (1992) Predictive value of symptoms of atypical depression for differential treatment outcome. *Journal of Clinical Psychopharmacology* 12: 197-202 utilizes stepwise multiple regression to analyze for predictors of differential response of depressed patients to placebo, imipramine, and phenelzine.

BR. Nagayama, H., et. al. (1991) Prediction of efficiacy of antidepressants by 1-week test therapy in depression. *Journal of Affective Disorders*, 23: 213-216 investigates predictive ability of baseline severity, Hamilton rating scale factors, and the Beckman rating scale factors which respect to clomimpramine treatment.

BS. Nierenberg, A.A., et.al.; (1991) Methodological considerations for the study of treatment-resistant depression. In Amsterdam: J.D., editor, *Refractory Depression* , vol. 2 of *Advances in Neuropsychiatry and Psychopharmacology*, pp. 1-12, Raven Press, Ltd., New York (will be provided under separate cover).

BT. Pande, A., et.al. (1988) Predictors of response to electroconvulsive therapy in major depressive disorder. *Biological Psychiatry* 24: 91-93 attempts to identify factors which

are predictive of a favorable outcome to electroconvulsive therapy.

BU. Paykel, E.S. (1972) Depressive typologies and response to amitriptyline. *British Journal of Psychiatry* 120: 147-156 discusses the use of typology in a depressive sample to predict outcome of a treatment with amtriptyline.

BV. Popescu, C., et.al. (1993). Predictors of the response to tricyclic antidepressants in major depression. *Roman Journal of Neurology and Psychiatry,* 31: 117-134 (will be provided under separate cover).

BW. Quitkin, F. M., et.al.; (1984) Identification of true drug response to antidepressants. *Arch. Gen. Psychiatry* 41: 782-786 (will be provided under separate cover).

BX. Quitkin, F. M., et.al.; (1987) Use of pattern analysis to identify true drug response: A replication .*Arch. Gen. Psychiatry* 44: 259-264 (will be provided under separate cover).

BY. Quitkin, F.M., et.al.; (1993) Columbia Atypical Depression ,*British Journal of Psychiatry* **163 (suppl. 21)**: 30-34 studies the response of patients to imipramine, phenelzine, and placebo.

BZ. Rao, C.R. (1973). *Linear Statistical inference and its applications.* Wiley Series in probability and mathematical statistics. Wiley, New York, 2nd edition. A Wiley-Interscience publication, pp. 172-173, 220-231, and 432-433 provide background on a mathematical method..

CA. Raskin, A. and Crook, T.A. (1976) The endogenous-neurotic distinction as a predictor of response to antidepressant drugs. *Psychological Medicine* 6: 59-70 performs an inverse factor analysis and determines that their are four patient types among depressed inpatients.

CB. Rumelhart, D. E. , et. al. (1986) Learning representations by back-propagating errors. *Nature* 323: 533-536 provides background aon a mathematical method.

CC. Samson, J. A., et. Al. (1994) Urinary MHPG and clinical symptoms in patients with unipolar depression. *Psychiatry Research* 51:157-165 investigates the relationship between urinary levels of MHPG and symptom scores on the Hamilton rating scale.

CD. Sauer, H., et.al. (1986) Prediction of the amitriptyline response: Psychopathology versus neuroendocrinology. *International Clinical Psychopharmacology* 1: 284-295 (abstract only) investigates the relationship between symptomology anddrug response outcome.

CE. Simpson, G.M., et.al. (1976) Two doses of imipramine in hospitalized endogenous and neurotic depressions. *Archives of General Psychiatry* 33 (will be provided under separate cover).

CF. Sotsky,S. M., et. al. (1991) Patient predictors of response to psychotherapy and pharmacotherapy: Findings in the NIMH treatment of depression collaborative research program. *American Journal of Psychiatry,* **148**: 997-1008 investigates patient characteristics predictive of treatment outcome.

CG. Vallejo, J., et. Al. (1991) Predictors of antidepressant treatment outcome in melancholia: pyschosocial, clinical, and biological indicators. *Journal of Affective Disorders*, **21:** 151-162 discusses predictive variables of response to imipramine and phenelzine at 6 weeks and at 6 months.

CH. Werbos, P.J. (1974) *Beyond Regressions: New Tools for Prediction and Analysis in the Behavoiral Sciences.* Ph.D. Thesis, Harvard University, Chapter (will be provided under separate cover).

CI. White, K. and White, J. (1986) Tranylcypromine: Patterns and Predictors of Response. *Journal of Clinical Psychiatry,* 47: 380-382 investigated what symptoms are predictors of positive outcome with tranylcypromine.

CJ. Georgotas, Anastasios, et al. (1987) Clinical Predictors of Response to Antidepressants in Elderly Patients. *Biol. Psychiatry* 22: 733-740 presents findings that not one of 21 variables representing symptoms, traits, or charateristics of the depressive illness were found to be significant predictors of antidepressant response.

Neither Applicant nor her agent make any representation that more pertinent art does not exist. It is anticipated that the Examiner will conduct a thorough search of the art and will carefully consider the documents cited herein.

Early consideration and allowance of the application is respectfully requested.

Respectfully submitted,

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